Title: Great Expectations—Ethics, Avian Flu, and the Value of Progress

Keywords: Censorship; Openness; Bioethics; Avian Influenza; Scientific Freedom

Word Count (manuscript only): 3,733

ABSTRACT

A recent controversy over the United States National Science Advisory Board for Biosecurity's recommendation to censor two publications on genetically modified H5N1 avian influenza has generated concern over the threat to scientific freedom such censorship presents. In this paper, I argue that in the case of these studies, appeals to scientific freedom are not sufficient to motivate a rejection of censorship. I then use this conclusion to draw broader concerns about the ethics of dual-use research.

INTRODUCTION

In November 2011, Ron Fouchier, a virologist from Erasmus University in the Netherlands, announced that he had successfully created a strain of H5N1 avian influenza that could be transmitted between ferrets simply by placing them in the same enclosure. Fouchier claimed that this study (hereafter, this and a similar study from the University of Wisconsin will be referred to as "the H5N1 studies") demonstrated that bird flu, a virus with a reported fatality rate of 59%,[i][1] could be engineered to become airborne and transmissible between humans. Though avian influenza presently does not undergo regular human-human transmission, the potential for the disease to evolve or be altered to do so presents a grave risk. The National Science Advisory Board for Biosecurity (NSABB) in the United States recommended the research be partly censored to prevent misuse of the research; their initial recommendation was that the studies be published without their complete methodology and would include a discussion of the public health impact of the research.[4]

The H5N1 studies are paradigmatic examples of the so-called *dual-use dilemma,* when scientific research, materials or technologies can be used to both benefit and harm humanity.[5, 6] Though dual-use research is not a new phenomenon (e.g., debates about the uses of nuclear science), the potential for the contemporary life sciences to both improve and diminish the quality of human life on a large scale has led to renewed interest in the ethical use of science and technology. The H5N1 studies are particularly concerning because, in addition to any benefits they may provide, they present a grave threat to global health and security.

Central to the debate following the NSABB's recommendation are the effects of censorship on *scientific freedom and progress*; the need for scientists to conduct and publish their work without

[i] This rate is of course contested, and during the debate on the H5N1 studies was contested numerous times. However, recent work has indicated that the 59% rate is—if not definitive [2]—a good estimate of the fatality rate.[3]

external interference, and the benefits this freedom provides.[7, 8] It is my overall contention that appeal to the value of scientific freedom or progress cannot provide sufficient reason not to—at least partially—censor the H5N1 studies, and the reasons for this are applicable to the wider debate about dual-use research.

This paper, then, will proceed as follows. First, I provide a brief history of the controversy to better engage with the substantive ethical issues presented by this dual-use research. I then critique the claims about the value of scientific freedom—and the relation of said freedom to the costs and benefits of dual-use research—made by opponents of the NSABB's initial recommendations, and finally, offer some general comments on scientific freedom and progress as they relate to dual-use research.

A (BRIEF) HISTORY OF THE CONTROVERSY

Fouchier first presented the results of his team's work on the potential for antigenic drift of the subtype of avian flu found in Indonesia at the European Scientific Working group on Influenza in Malta, September 2011. Fouchier and his team:

> …introduced mutations, under strict laboratory safety procedures, by reverse genetics into laboratory ferrets. They then collected a nasal wash from each infected ferret and inoculated another ferret after a few days. They repeated this process ten times. The result? H5N1 had been transmitted to three out of four ferrets. "This virus is airborne and as efficiently transmitted as the seasonal virus," said Fouchier. His research team found that only 5 mutations, 3 by reverse genetics and 2 by repeated transmission, were enough to produce this result.[9]

These five mutations, taken together, resulted in the creation of a highly virulent strain of H5N1. All five mutations are present in nature, though they have never been seen in a single virus at the same time.[7] Yoshihiro Kawaoka, of the University of Wisconsin, conducted an experiment that achieved similar results. Paul Keim, acting head of the NSABB, described the Kawaoka paper:

> They demonstrate the compatibility of segments of the 2009 pandemic influenza (A(H1N1)pdm09) backbone with H5 haemagglutinin [which binds the virus to the cells to be infected] (HA) to produce a virus that can be transmitted between ferrets.[4]

Both papers result in a strain of H5N1 that is highly transmissible in ferrets. Ferrets are used in virology as a model for the human immune response to influenza.[10] According to Fouchier,[7] these strains of H5N1 are thus likely to be transmissible through air in humans.

The studies caused a significant amount of attention in November 2011, when the NSABB met to debate whether the studies should be published. In December, the NSABB announced its recommendations against publication of the studies.[4] Meetings were convened both in the United States and in Geneva to discuss the recommendation, and a moratorium against research into avian influenza was announced on January 20, 2012.

On the 30th of March the NSABB revised their decision, and approved publication of revised manuscripts prepared by both teams.[11] Kawaoka's study was approved unanimously after Kawaoka supplied a revised manuscript, as the discovery of haemagglutinin binding as an important pathway in mammalian flu was considered of great public health benefit.[12] Fouchier's study was approved by a 12-6 ruling of the NSABB for two reasons. First, Fouchier revised his manuscript to not include the specific genetic mutations needed for the modified flu to be created.[11] Second, lack of harmonised oversight between the Netherlands and U.S.A. made distribution information to vetted parties impossible,[13] combined with the possibility of the dual-use information being leaked online.[12]

However, this should only increase our interest in the H5N1 studies as a case study in dual-use bioethics. An analysis of the assessment the NSABB underwent is vital, both to better understand how ethical decision-making is occurring in practice about dual-use research, and to critique this assessment as necessary.[14] Further, assessing the claims made in the debate will give us a better

understanding of the types of claims made both for and against censoring dual-use research, and improve on the quality of the debate in the future. In this article, I plan on assessing the argument that censoring science violates a scientist's (justified) freedom to conduct and disseminate their research, and the ways that this freedom is tied to the benefits of dual-use research—in this case, the putative benefits of the H5N1 studies.

GREAT EXPECTATIONS: THE CENSORSHIP DEBATE AND THE VALUE OF SCIENTIFIC FREEDOM

Fouchier's experiment—and the NSABB's reaction—attracted attention from health and biosecurity circles worldwide. Scientific and popular publications reported the views of a number of key figures in virology, biology and biosecurity circles;[4,7–8,15] with more joining in either through op-eds,[16] short articles,[17] or their own personal communiqués (e.g., blogs),[18–21] to debate the merits of restricting access to the results. These views continue to inform the character of the debate.

Simply put, the reasons for and against can be summed up as follows:

For Censorship:

1. The modified virus, should it accidently escape containment, could kill a very large number of people;
2. A malevolent actor could use the modified virus to kill a large number of people. [4,7,22]

Against Censorship:

1. Censorship violates principles of scientific openness and freedom;[5,18,17,23]
2. The benefits of the study to human health if the study is published:
    a. Enhancing awareness about H5N1 avian influenza;
    b. Enabling better pandemic flu surveillance;
    c. Enabling better vaccine creation;[7]
3. Pragmatic difficulties in censoring science, such as government overreach,[21] incentivising subversive activity, our ability to reliably censor information stored and communicated

electronically, or the inevitability of scientific discoveries outpacing attempts to suppress them.[14]

In the interest of brevity I will not examine pragmatic difficulties with censorship in this paper, except to describe them here for the sake of completeness. There are concerns that even if there is some dual-use research whose potential for misuse is so great as to outweigh the value of protecting scientific freedom, censorship itself is a misguided policy due to the nature of censorship *in practice*. Censorship has an ugly history, and suggestions to suppress information are—reasonably, I think—met with suspicion. There is also growing belief that securing information is hazardous in the modern world of computing—either because information cannot be secured, or because the attempt at securing information only provokes more drive to discover that which others deem too dangerous to be known widely.[20]

I won't deal with these here. However, I don't believe they undermine my analysis—even if in the final analysis censorship of dual-use research as a policy is not feasible. Whatever form or combination of regulatory strategies are ultimately implemented in the life sciences, there will be a need to weigh the value of these strategies against any freedoms that are infringed upon as a result of regulation. With this in mind, I will focus on the first two critiques of the censorship of the H5N1 studies: namely, that censorship violates scientific openness and freedom, and prevents the realisation of valuable benefits to human health.

Freedom

On the face of it, there seem to be four things we are trying to get at, either individually or together, when we raise an objection like censorship "violates scientific freedom/openness." Recall that I take scientific freedom to be the freedom to publish scientific information without interference. What I am interested in is the moral weight this carries, or should carry, in debates about dual-use research.

First, we might think that scientific freedom is good for its own sake; given two otherwise identical worlds, the world with scientific openness (or more scientific openness) is simply better than the

world without (or with less) scientific openness. But this does not seem a factor that can, on its own, justify publication of the H5N1 studies. Even if scientific freedom is valuable for its own sake, it is surely not more valuable than preventing mass casualties in the event of the release, accidental or deliberate, of modified H5N1.

More plausibly, we might think that science requires freedom and openness to function properly for three reasons: i) to confirm and replicate results; ii) build on existing scientific knowledge to create new knowledge and progress science; iii) to claim priority over a discovery.[24] I will show that these reasons are not enough to defend H5N1 against censorship.

It is not clear that confirming results necessitates complete openness. The NSABB originally proposed that vetted scientists be allowed access to the full H5N1 studies to confirm and replicate the results. [10,14] This could, if designed properly, allow control over who has access to the results, promoting biosafety and biosecurity without sacrificing the validity of the results.

Moreover, there is a good reason to restrict access *because* of the possibility of the study being replicated. For every successful replication of the result, there is a chance the created strain of H5N1 will escape containment; the more times the experiment is repeated, the more chance of a catastrophic outcome.[25] It is prudent, qualified by the need to do good science, to limit not just who reproduces the studies, but how often these studies are reproduced.

The second claim is that scientific freedom and openness are essential to the structure of science. Put another way: in order to create valuable knowledge, we need to ensure science is open and free. Particularly if we believe we have little prior knowledge of where innovative and beneficial research will arise, maximising openness maximises the chance of reaping the benefits of new research.[26]

However, it seems that rejecting regulation based on the uncertainty of how science will progress possess limited force as a justification. On the broadest level, significant effort is put into funding allocation to decide which projects and scientists will produce the best results. These systems are

subject to their own critique; nevertheless, they show that we can and do have certain expectations about where good research will occur and what research should be done. If such judgements are plausible in deciding what science should be done, why not in whom we allow to access the H5N1 studies? There is a clear trade-off between security and progress here, but it is one that we can vary as circumstances fit.

By way of example, the Manhattan project saw scientific and technological advancements of considerable sophistication (i.e., the building of an atomic bomb) that required novel knowledge creation in areas of quantum mechanics, shock physics, metallurgy, early computational science, and materials science. This work was pursued in highly classified community, yet allowed for results to be reliable and progress to be made with limited openness.[27] Extra openness may add an extra layer of security in establishing knowledge about the world; but it is not at all clear that this epistemic security is so important that it would always, on reflection, outweigh other concerns of physical security.

The claim that openness is valuable because it leads to scientific progress seems *prima facie* true—we might think that progressing scientific knowledge is valuable for its own sake, independent of the use of that knowledge. We also value the material benefits we gain from that knowledge in terms of health and other important goods. That requires further inquiry, which I will turn to in the next section.

Yet scientific progress, whether for the sake of new knowledge or other gains, it is not the only thing we care about. Researchers already accept certain restrictions on what information they may disseminate. For example, we generally believe that it is impermissible, on moral grounds, to release the personal information and identities of human research subjects. I suspect we would think this is so even if doing so would lead to more scientific knowledge and progress. It is permissible for a journal to prevent the publications of information and identifies of research participants because openness of this kind would violate the privacy of individuals. The value of

respecting the privacy of experimental subjects, in this case, outweighs the value promoted through publication. It doesn't seem that we would abandon this or any other fundamental element of medical bioethics solely on the consideration of progress. It isn't clear, then, why progress should outweigh other considerations in this dual-use dilemma without knowing a little more about what type of progress we are talking about, and examine the consequences of pursuing that progress.

Finally, openness clearly benefits researchers by allowing them to claim priority over scientific discoveries, leading to material and status gains in the process. But one would be hard pressed to justify that the status gained by scientists would be so valuable as to outweigh the potential malevolent uses of the modified H5N1 virus.[ii] Moreover, if we take considerations of status seriously, a large amount of status could be lost if the publications were released and a mass casualty event like a bioterror attack then occurred. The reputations of nuclear scientists, for example, have suffered from a litany of malevolent uses, reckless practices, unforseen accidents and lack of public education that hamper the development of the field outside of classified laboratories. It is likely the biological sciences would likewise suffer a great blow to their standing if bio-weapons attacks occurred.

Benefits and Costs

In the last section, I argued that if one wanted to justify publishing the H5N1 studies one would have to demonstrate that the value of scientific freedom outweighed the potential harm that could occur through malevolent use of the research. So far, I have argued that justifications based on the value of scientific freedom do not meet that challenge. One could argue, however, that the benefits of the H5N1 studies in terms of their contribution to medicine and public health really do outweigh the potential dangers. I will now argue against that possibility, based on the three main claims made about the benefits of these studies: that it 1) alerts the community about the dangers of H5N1, 2) enables disease surveillance, and 3) enables vaccine production.

[ii] Though surely Fouchier has become more famous through the censorship controversy than if the controversy didn't exist—more famous than through merely establishing priority.

To the first claim, we should ask first to whom we refer when we talk of alerting "the community". If by "the community" we mean the public, then the current controversy alone has achieved this goal. The announcement of the results, and the recommendation to censor the methodology were sufficient to raise awareness of the danger. Moreover, it seems unlikely that the methodological details of the H5N1 studies—the details of most concern—are useful to the public for the purpose of raising awareness.

This argument is even less convincing if by "community" we mean scientists or security experts. Scientists are clearly concerned about the risk of pandemic flu—Fouchier's presentation in Malta was during a session on pandemic potentials. Security experts and governments are likewise taking action, evidenced by the estimated $6.42 billion allocated by the U.S. to biodefence for the 2012 financial year, up from $5b in 2010 and despite U.S. economic turmoil.[28]

When it comes to disease surveillance, there is the question of whether the information contained in the studies could be useful. It has been argued that there is no guarantee that an emerging human transmissible strain of H5N1 will be the same as the strains created in the H5N1 studies.[4,15] This would then undercut the value of the studies vis-à-vis surveillance. Keim has argued further that because of this possibility, these studies could in fact be counterproductive to surveillance.[4]

Vaccines run into similar problems. Similar to the argument against the value of the research for surveillance, it is not clear that the strains described in this research will match evolutionary pathways that occur in nature.[4,15] As with surveillance, it may be counterproductive to focus our vaccination efforts on lab-created strains.

However, *even if technically plausible*, surveillance and vaccine distribution rely on political, social, ethical, and technical factors that may not presently exist. The claims made about the benefit of science are *ethical* claims—that is, they are claims about what is morally valuable in life, such as health—but moreover are ethical claims about the consequences of research. However, in order to

bring these consequences about—in order to gain the benefits of improved disease surveillance or vaccine production and distribution—one has to have institutions that actually further this goal. If not, the chance that this beneficial state of affairs will occur is minimal.

As it stands, the political will to institute widespread public health measures within nations, much less globally, is small.[29] That is, even in developed nations there are continuing and protracted political debates about the allocation of funding, structure, and use of public health institutions.[30] The likelihood that the H5N1 studies will actually bring about a good state of affairs, then, is proportionately decreased compared to if public health received strong and widespread support. Claims to the utility of surveillance tools or vaccines that emerge from this research are just as contingent as, say, the chances that someone will use the research to commit an act of bioterrorism.

Moreover, there are serious differences in public health responsiveness between nations. We therefore run the risk—assuming that these benefits obtained— of protecting ourselves at the cost of more vulnerable populations. Consider the event of an attack using the modified H5N1 virus. There is little chance it will remain contained in a particular geographic area. Developed population centres will likely suffer from an outbreak; developing nations could be devastated. Even if we believed it was likely these advances could benefit certain communities on a local scale, the harms posed are global and severe.

As beneficial as we might find the research, it is unlikely that the H5N1 studies will provide any near-term benefit for the population at large. The institutions and infrastructure on which those benefits depend are not likely to materialise without significant effort. Moreover, even if we succeed in developing this infrastructure on a local level (e.g. within the USA), those populations that experience the worst of bird flu—typically developing nations with poor public health measures—are left vulnerable.

CONCLUSION: THE VALUE OF PROGRESS

I have provided a series of considerations we might think motivate a defence against censorship of the H5N1 studies. The strongest is that of the value of scientific progress, but in case of the H5N1 studies this appeal is unsuccessful. Nonetheless, it is this claim regarding the value of progress that is the most interesting, and one we should reflect on.

Censorship of dual-use research such as the H5N1 studies, I have shown, is a complex issue. The gains we make through science exist, but are not always straightforward or immediate. Scientific progress can bring us gains in knowledge, and this is surely valuable. But the value of knowledge is—at least in the near-term—overshadowed by the potential for that knowledge to aid or diminish our ability to solve problems that impact on human lives in concrete ways, such as health. Yet these larger, more tangible benefits, on the other hand, are reliant on contingent factors that may not exist.

This is a distinctly *ethical* decision making process.[5] Moreover, it is unlikely that such a process is one that should be governed exclusively by scientists. There are detailed technical issues involved in dual-use dilemmas that those scientists in the field (in the H5N1 studies, influenza research) can and should bring their expertise to. But considerations of value will require other expert (e.g., public health, ethics, and economics) and community participation. Scientists may approach their research with the best of intentions and the good of society in mind, but it would be a mistake to assume that they could know what is best for the world—and a tragedy to foist that burden on them.

Creating good justifications for pursuing and publishing dual-use scientific research relies on conceiving of the benefits of scientific research honestly and pluralistically. Scientific progress clearly relies on existing scientific research, and in that sense we could deprive ourselves of potentially beneficial advances for as long as we censor the H5N1 studies. But the *value* of those advances is not simply tied to previous research, but to contingent facts about the world too easily ignored. In this way, some scientific research outpaces our ability to benefit from it. This might not

be a problem when the research is (or is mostly) benign. But when we consider dual-use research like the H5N1 studies, it should give us pause.

REFERENCES

1 WHO. Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2012. http://www.who.int/influenza/human_animal_interface/avian_influenza/EN_GIP_20120326CumulativeNumberH5N1cases.pdf (accessed 30 Mar 2012)

2 Khuntirat, B.P., Yoon, I, Blair, P.J. et. al. Evidence for Subclinical Avian Influenza Virus Infections Among Rural Thai Villagers. *Clin Infect Dis* 2011;**53**:e107-e116

3 Nasreen S, Khan S.U., Azziz-Baumgartner E, et. al. Board 183. Sero-prevalence of H5N1 antibodies among poultry workers in Bangladesh, 2008-2009. ICEID program and abstract book, (presented 13 Mar 2012), p.116

4 Keim, P.S. Q&A: Reasons for proposed redaction of flu paper. *Nature* 2012;**482**:156–157 doi:10.1038/482156a

5 Miller, S, Selgelid, M.J. Ethical and Philosophical Considerations of the Dual-Use Dilemma in the Biological Sciences. Dordecht, NE:Springer 2008

6 Selgelid, M.J. A Tale of Two Studies: Ethics, Bioterrorism and the Censorship of Science. *Hastings Cent Rep* 2012;**37**:35–43

7 Enserink, M. Scientists Brace for Media Storm Around Controversial Flu Studies. *Science Insider* 23 Nov 2011. http://news.sciencemag.org/scienceinsider/2011/11/scientists-brace-for-media-storm.html (accessed 30 Mar 2012)

8 Enserink, M. Grudgingly, Virologists Agree to Redact Details in Sensitive Flu Papers. *Science Insider* 20 Dec 2011. http://news.sciencemag.org/scienceinsider/2011/12/grudgingly-virologists-agree-to.html (accessed 30 Mar 2012)

9 European Scientific Group on Influenza. The Influenza Times Conference Newsletter 11-14 September 2011. http://www.eswiconference.org/Downloads/FEIC_news_1.aspx (accessed 30 Mar 2012)

10 NSABB. National Science Advisory Board for Biosecurity Recommendations November 21, 2011. http://www.aaas.org/news/releases/2011/media/1220herfst_nsabb_rec.pdf (accessed 30 Mar 2012)

11 NSABB. March 29-30, 2012 Meeting of the National Science Advisory Board for Biosecurity to Review Revised Manuscripts on Transmissibility of A/H5N1 Influenza Virus. http://oba.od.nih.gov/oba/biosecurity/PDF/NSABB_Statement_March_2012_Meeting.pdf (accessed 2 April 2012)

12 Butler, D., Ledford, H. US biosecurity board revises stance on mutant-flu studies. *Nature Breaking News* 30 March 2012 http://www.nature.com/news/us-biosecurity-board-revises-stance-on-mutant-flu-studies-1.10369 (accessed 31 Mar 2012)

Nicholas Evans 10/10/12 9:01 PM
Deleted: 2012

Nicholas Evans 10/10/12 9:03 PM
Deleted: 2012

13 Branswell, H. US biosecurity panel clears publication path for controversial bird flu studies. *Winnipeg Free Press* 30 Mar 2012. http://www.winnipegfreepress.com/world/us-biosecurity-panel-clears-publication-path-for-controversial-bird-flu-studies-145213375.html (accessed 31 Mar 2012).

14 Letter from Michael Osterholm to Amy Patterson, 12 April 2012.

15 Kwek, G. Armageddon super virus recipe: keep secret or publish? *Sydney Morning Herald* 6 Dec 2011. http://www.smh.com.au/technology/sci-tech/armageddon-super-virus-recipe-keep-secret-or-publish-20111206-1og76.html#ixzz1qYs8l5u3 (accessed 30 Mar 2012)

16 Caplan, A. When censoring science makes sense. *CNN* 22 Dec 2011. http://edition.cnn.com/2011/12/21/opinion/caplan-flu-science/index.html (accessed 20 Mar 2012)

17 Palese, P., Wang, T.T. H5N1 influenza viruses: Facts, not fear. *Proc. Natl. Acad. Sci. U.S.A.* 25 Jan 2012 (online). Doi:10.1073/pnas.1121297109

18 Racaniello, V. Ferreting out influenza H5N1 6 Dec 2012. http://www.virology.ws/2011/12/06/ferreting-out-influenza-h5n1/ (accessed 30 Mar 2012)

19 Racaniello, V. H5N1 facts, not fear. http://www.virology.ws/2012/01/25/h5n1-facts-not-fear/ (accessed 30 Mar 2012)

20 Carlson, R. Censoring science is detrimental to security. http://www.synthesis.cc/2012/01/censoring-scientific-publication-is-detrimental-to-security.html (accessed 30 Mar 2012)

21 Eisen, M. Stop the presses! H5N1 Frankenflu is going to kill us all! http://www.michaeleisen.org/blog/?p=801 (accessed 30 Mar 2012)

22 Berns, K.I., Casadevall, A., Cohen, M.L. et. al. Policy: Adaptations of avian flu virus are a cause for concern. *Nature* 2012;**482**:153–154 doi:10.1038/482153a

23 The New York Academy of Sciences. Dual-use research: H5N1 Influenza Virus and Beyond. December 2011 http://www.nyas.org/Publications/EBriefings/Detail.aspx?cid=4cd6eec7-7bbf-4be8-b9d3-b458937c043d (accessed 30 mar 2012)

24 National Research Council. Biotechnology Research in an Age of Terrorism. Washington, DC: National Academies Press 2004.

25 Garret, L. The Bioterrorist Next Door. *Foreign Policy* 15 Dec 2011. http://www.foreignpolicy.com/articles/2011/12/14/the_bioterrorist_next_door?page=full (Accessed 20 Dec 2011)

26 Bush, V. Science: The Endless Frontier. Washington D.C.: United States Government Printing Office 1945

27 Rhodes, R. The Making of the Atomic Bomb. New York, NY: Simon and Schuster 1995.

28 Franco, C., Sell, T.K. Federal Agency Biodefense Funding, FY2011–FY2012. *Biosecur Bioterror* 2011;**9**:117–137

29 Garrett, L. Betrayal of Trust: The Collapse of Global Public Health. New York, NY: Hyperion 2001.

30 Butler, Declan. Flu surveillance lacking. *Nature* 2012;**483**:520-522